Supplementary Material

"Variation of nonsynonymous/synonymous rate ratios at *HLA* genes over time and phylogenetic context"

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Table S1: Pairwise estimations for substitution rates (NR data sets)

		non-ARS					ARS				
Locus	Quantile[a]	$\overline{dN}$	$\overline{dS}$	$\overline{\omega}$[b]	$\overline{dN}/\overline{dS}$	dN>dS[d]	$\overline{dN}$	$\overline{dS}$	$\overline{\omega}$	$\overline{dN}/\overline{dS}$	dN > dS
HLA-A		**0.01[c]**	**0.05**	**0.36**	**0.36**	**449(8.38%)**	**0.11**	**0.07**	**1.37**	**1.62**	**5356(75.99%)**
	1	0.00	0.01	0.38	0.50	449	0.03	0.03	0.91	1.25	877
	2	0.02	0.06	0.33	0.32	0	0.13	0.07	1.38	1.82	1684
	3	0.02	0.05	0.36	0.35	0	0.13	0.08	1.37	1.66	1800
	4	0.02	0.08	0.30	0.30	0	0.14	0.08	1.56	1.76	1160
HLA-B		**0.01**	**0.04**	**0.33**	**0.30**	**121(4.97%)**	**0.12**	**0.10**	**1.27**	**1.19**	**1637(65.87%)**
	1	0.01	0.01	0.47	0.48	121	0.08	0.07	1.32	1.19	392
	2	0.01	0.03	0.36	0.36	0	0.13	0.13	0.97	0.94	336
	3	0.01	0.04	0.28	0.28	0	0.14	0.12	1.42	1.20	419
	4	0.01	0.06	0.24	0.24	0	0.14	0.09	1.40	1.55	490
HLA-C		**0.02**	**0.05**	**0.39**	**0.38**	**434(7.24%)**	**0.07**	**0.03**	**1.00**	**2.53**	**4749(79.22%)**
	1	0.00	0.01	0.48	0.52	434	0.03	0.02	0.89	1.38	928
	2	0.01	0.04	0.32	0.32	0	0.07	0.03	0.96	2.82	1267
	3	0.02	0.06	0.41	0.42	0	0.08	0.03	1.11	2.87	1282
	4	0.03	0.08	0.37	0.37	0	0.09	0.03	1.08	2.94	1266

a, quantiles of divergence ($dS_{non\text{-}ARS}$).

b, average pairwise dN/dS.

c, bold refers to the average pairwise values for each locus.

d, percentages correspond to the proportion of pairs for which dN > dS in relation to the total number of pairwise comparisons.

NR, non-recombinant data set

Table S2: Likelihoods for site models

Locus	l_1	l_2	$2(l_2 - l_1)$	l_7	l_8	$2(l_8 - l_7)$
HLA-A	-4361.1(-3537.1)	-4217.2(-3386.9)	287.9*(180.5*)	-4374.7(-3538.6)	-4218.5(-3386.6)	312.3*(190.9*)
HLA-B	-6969.1(-3537.1)	-6624.9(-3386.9)	180.4*(300.4*)	-6986.5(-3541.6)	-6632.8(-3386.6)	190.9*(310*)
HLA-C	-3634.1(-3256.9)	-3562.1(-3257.5)	144*(-1.2)	-3635.5(-3257.9)	-3562.7(-3204.5)	145.6*(106.8*)

NOTE.- $l_1$and l_2, negative log likelihoods for models M1 and M2 (the same applies to models M7 and M8);

*$P < 0.01$; d.f.=2

Numbers in parenthesis refer to the equivalent estimates for NR datasets.

Table S3: Site models likelihood convergence for *HLA*-A (R)

Model	Initial ω	Initial κ	M1	M2	M2*vs*M1	M7	M8	M8*vs*M7
Fequal	0.2	2	-4476.54	-4267.42	*	-4480.98	-4267.47	*
	0.4	2	-4476.54	-4267.42	*	-4483.70	-4266.10	*
	0.6	2	-4476.54	-4265.98	*	-4479.93	-4265.99	*
	0.8	2	-4476.54	-4266.09	*	-4479.90	-4266.11	*
F1x4	0.2	2	-4450.86	-4259.73	*	-4456.03	-4259.88	*
	0.4	2	-4450.86	-4259.73	*	-4459.38	-4259.88	*
	0.6	2	-4450.86	-4259.73	*	-4456.03	-4259.88	*
	0.8	2	-4450.86	-4259.73	*	-4456.03	-4259.88	*
F3x4	02	2	-4361.10	-4217.16	*	-4374.67	-4218.53	*
	0.4	1	-4361.10	-4217.16	*	-4374.67	-4218.53	*
		2	-4361.10	-4217.16	*	-4374.67	-4218.53	*
	0.6	2	-4361.10	-4217.16	*	-4374.67	-4218.53	*
	0.8	2	-4361.10	-4217.16	*	-4374.67	-4218.53	*
F61	0.2	2	-4320.43	-4192.21	*	-4336.08	-4194.25	*
	0.4	2	-4320.43	-4192.21	*	-4336.08	-4194.25	*
	0.6	2	-4320.43	-4192.21	*	-4336.08	-4194.25	*
	0.8	2	-4320.43	-4192.21	*	-4336.08	-4194.25	*

* significant LRT ($P < 0.05$).

NOTE.- k, the transition/transversion rate ratio; Fequal, all codons have the same frequency; F1x4, codon frequencies based on the frequencies of each nucleotide; F3x4, codon frequencies based on the frequencies of each nucleotide in each codon position; F61, each codon frequency is a free parameter. R, data set with recombinants.

Table S4: Site models likelihood convergence for *HLA-A* (NR)

Model	Initial ω	Initial κ	M1	M2	M2*vs*M1	M7	M8	M28*vs*M7
Fequal	0.2	2	-3701.92	-3491.17	*	-3701.97	-3491.30	*
	0.4	2	-3701.92	-3491.17	*	-3701.97	-3491.30	*
	0.6	2	-3701.92	-3500.97	*	-3702.03	-3491.30	*
	0.8	2	-3701.98	-3491.15	*	-3701.97	-3491.28	*
F1x4	0.2	2	-3668.14	-3464.40	*	-3675.15	-3464.41	*
	0.4	2	-3668.14	-3475.11	*	-3668.30	-3464.45	*
	0.6	2	-3668.14	-3464.40	*	-3668.30	-3464.41	*
	0.8	2	-3668.14	-3475.11	*	-3675.15	-3464.41	*
F3x4	02	2	-3537.14	-3386.90	*	-3538.56	-3386.57	*
	0.4	1	-3537.14	-3386.90	*	-3541.58	-3386.57	*
		2	-3537.14	-3386.90	*	-3538.56	-3386.57	*
	0.6	2	-3537.14	-3386.90	*	-3541.58	-3386.57	*
	0.8	2	-3537.14	-3386.90	*	-3538.56	-3386.57	*
Fcodon	0.2	2	-3473.08	-3334.39	*	-3484.42	-3333.90	*
	0.4	2	-3473.08	-3334.39	*	-3474.05	-3333.90	*
	0.6	2	-3473.08	-3334.39	*	-3474.05	-3333.90	*
	0.8	2	-3473.08	-3334.39	*	-3474.05	-3333.90	*

* significant LRT ($P < 0.05$).

NOTE.- k, the transition/transversion rate ratio; Fequal, all codons have the same frequency; F1x4, codon frequencies based on the frequencies of each nucleotide; F3x4, codon frequencies based on the frequencies of each nucleotide in each codon position; F61, each codon frequency is a free parameter. NR, data set after removal of recombinants.

Table S5: Site models likelihood convergence for *HLA-B* (R)

Model	Initial ω	Initial κ	M1	M2	M2*vs*M1	M7	M8	M8*vs*M7
Fequal	0.2	2	-7228.90	-6760.75	*	-7274.97	-6753.2	*
	0.4	2	-7228.98	-6751.69	*	-7251.21	-6753.9	*
	0.6	2	-7227.86	-6752.46	*	-7239.66	-6754.86	*
	0.8	2	-7228.98	-6751.69	*	-7240.78	-6755.04	*
F1x4	0.2	2	-7222.87	-6767.71	*	-7234.06	-6771.06	*
	0.4	2	-7226.59	-6767.08	*	-7236.79	-6771.00	
	0.6	2	-7223.55	-6767.71	*	-6767.71	-6771.62	
	0.8	2	-7227.79	-6767.08	*	-7233.72	-6771.99	*
F3x4	02	2	-6966.73	-6623.72	*	-6984.45	-6934.37	*
	0.4	1	-6970.05	-6624.89	*	-6983.14	-6632.79	*
		2	-6969.08	-6624.88	*	-6986.54	-6632.79	*
	0.6	2	-6969.88	-6624.88	*	-6981.93	-6633.68	*
	0.8	2	-6966.54	-6625.24		-6983.3	-6632.79	*
Fcodon	0.2	2	-6862.47	-6535.93	*	-6876.08	-6547.08	*
	0.4	2	-6860.18	-6539.27	*	-6872.78	-6548.52	*
	0.6	2	-6861.53	-6537.12	*	-6903.90	-6549.89	*
	0.8	2	-6860.6	-6537.12	*	-6905.63	-6543.72	*

* significant LRT ($P < 0.05$).

NOTE.- k, the transition/transversion rate ratio; Fequal, all codons have the same frequency; F1x4, codon frequencies based on the frequencies of each nucleotide; F3x4, codon frequencies based on the frequencies of each nucleotide in each codon position; F61, each codon frequency is a free parameter. R, data set with recombinants.

Table S6: Site models likelihood convergence for *HLA-B* (NR)

Model	Initial ω	Initial κ	M1	M2	M2*vs*M1	M7	M8	M8*vs*M7
Fequal	0.2	2	-3701.98	-3491.17	*	-3701.97	-3491.30	*
	0.4	2	-3702.11	-3491.15	*	-3702.03	-3491.28	*
	0.6	2	-3701.92	-3491.155	*	-3702.03	-3491.30	*
	0.8	2	-3701.92	-3491.155	*	-3707.27	-3491.28	*
F1x4	0.2	2	-3668.84	-3464.4	*	-3668.30	-3464.41	*
	0.4	2	-3668.14	-3464.4	*	-3668.30	-3464.45	*
	0.6	2	-3668.14	-3464.43	*	-3668.30	-3464.41	*
	0.8	2	-3668.14	-3475.11	*	-3668.30	-3464.41	*
F3x4	02	2	-3537.14	-3386.90	*	-3547.78	-3386.57	*
	0.4	1	-3537.14	-3386.90	*	-3541.59	-3386.57	*
		2	-3537.14	-3386.90	*	-3541.58	-3386.57	*
	0.6	2	-3537.14	-3386.90	*	-3541.58	-3386.57	*
	0.8	2	-3537.14	-3386.90	*	-3541.58	-3386.57	*
Fcodon	0.2	2	-3473.08	-3334.39	*	-3475.46	-3333.90	*
	0.4	2	-3473.08	-3334.39	*	-3474.05	-3333.90	*
	0.6	2	-3473.08	-3334.39	*	-3484.42	-3333.90	*
	0.8	2	-3473.08	-3334.39	*	-3475.46	-3333.90	*

* significant LRT ($P < 0.05$).

NOTE.- k, the transition/transversion rate ratio; Fequal, all codons have the same frequency; F1x4, codon frequencies based on the frequencies of each nucleotide; F3x4, codon frequencies based on the frequencies of each nucleotide in each codon position; F61, each codon frequency is a free parameter. NR, data set after removal of recombinants.

Table S7: Site models likelihood convergence for *HLA-C* (R)

Model	Initial ω	Initial κ	M1	M2	M2*vs*M1	M7	M8	M8*vs*M7
Fequal	0.2	2	-3697.36	-3603.67	*	-3698.94	-3603.92	*
	0.4	2	-3697.36	-3603.67	*	-3699.17	-3605.09	*
	0.6	2	-3697.36	-3606.20	*	-3697.52	-3767.94	
	0.8	2	-3697.36	-3602.37	*	-3697.52	-3602.61	*
F1x4	0.2	2	-3701.58	-3702.28		-3704.0	-3611.8	*
	0.4	2	-3701.58	-3702.29		-3701.95	-3611.8	*
	0.6	2	-3702.28	-3611.76	*	-3701.95	-3703.4	
	0.8	2	-3701.02	-3702.29		-3701.95	-3611.8	*
F3x4	02	2	-3633.59	-3634.21		-3636.53	-3562.82	*
	0.4	1	-3633.59	-3634.21		-3636.07	-3562.82	*
		2	-3634.08	-3562.14	*	-3635.49	-3562.73	*
	0.6	2	-3634.59	-3562.77	*	-3636.02	-3562.82	*
	0.8	2	-3634.08	-3562.14	*	-3638.35	-3636.18	
Fcodon	0.2	2	-3572.77	-3573.43		-3575.73	-3506.68	*
	0.4	2	-3572.77	-3505.98	*	-3575.73	-3506.68	*
	0.6	2	-3572.92	-3505.98	*	-3575.87	-3506.68	*
	0.8	2	-3572.77	-3505.98	*	-3575.73	-3506.68	*

* significant LRT ($P < 0.05$).

NOTE.- k, the transition/transversion rate ratio; Fequal, all codons have the same frequency; F1x4, codon frequencies based on the frequencies of each nucleotide; F3x4, codon frequencies based on the frequencies of each nucleotide in each codon position; F61, each codon frequency is a free parameter. R, data set with recombinants.

Table S8: Site models likelihood convergence for *HLA-C* (NR)

Model	Initial ω	Initial κ	M1	M2	M2*vs*M1	M7	M8	M8*vs*M7
Fequal	0.2	2	-3333.10	-3378.3		-3335.15	-3265.59	*
	0.4	2	-3333.13	-3265.59	*	-3334.89	-3265.59	*
	0.6	2	-3335.08	-3267.85	*	-3333.17	-3265.59	*
	0.8	2	-3333.10	-3267.85	*	-3334.87	-3265.59	*
F1x4	0.2	2	-3321.13	-3321.47		-3321.13	-3321.66	
	0.4	2	-3321.17	-3254.27	*	-3321.25	-3321.43	
	0.6	2	-3321.25	-3254.25	*	-3321.05	-3321.64	
	0.8	2	-3321.13	-3321.64		-3321.05	-3321.50	
F3x4	02	2	-3256.94	-3257.45		-3258.21	-3258.36	
	0.4	1	-3256.89	-3204.55	*	-3258.16	-3258.74	
		2	-3256.89	-3257.46		-3257.91	-3204.64	*
	0.6	2	-3256.89	-3204.49	*	-3257.87	-3258.66	
	0.8	2	-3256.94	-3257.26		-3257.91	-3204.50	*
Fcodon	0.2	2	-3204.57	-3164.9	*	-3205.78	-3208.89	
	0.4	2	-3204.57	-3154.39	*	-3205.78	-3154.55	*
	0.6	2	3204.57	-3205.05		-3205.78	-3206.28	
	0.8	2	3204.57	-3154.39	*	-3205.78	-3154.55	*

* significant LRT ($P < 0.05$).

NOTE.- k, the transition/transversion rate ratio; Fequal, all codons have the same frequency; F1x4, codon frequencies based on the frequencies of each nucleotide; F3x4, codon frequencies based on the frequencies of each nucleotide in each codon position; F61, each codon frequency is a free parameter. NR, data set after removal of recombinants.

Table S9: Classifications of ARS codons

Reference	Total number of codons
Bjorkman et al. (1987) (BJOR)	57
Chelvanayagam (1996) (CHEV)	48
Yang and Swanson (2002) (YANG)	26
BIT	33

BJOR and CHEV are ARS classifications.

YANG is a list of codons with significant $\omega > 1$ in *HLA* genes.

BIT is the set of codons with $P > 0.95$ (M8; see Methods for details).

Table S10: Parameter estimates under site models for *HLA-A*

Data set	Model	Parameter estimates	Sites with $\omega > 1$
R	M0	$\omega = 0.96$	None
	M1	$p_0 = 0.80$, $p = 0.2$, $\omega_0 = 0.05$, $\omega_1 = 1$	Not allowed
	M2	$p_0 = 0.68$, $p_1 = 0.25$, $p_2 = 0.07$	**9F,62Q,63E,66N,70H,76A,77N,81L**,82R,**97I,**
		$\omega_0 = 0.08$, $\omega_1 = 1$, $\omega = 9.12$	**99Y,114R**
	M7	$p = 0.08$, $q = 0.20$	Not allowed
	M8	$p_0 = 0.93$, $p = 0.09$, $q = 0.16$	**9F,62Q,63E,66N,70H,76A,77N,81L,**82R,95I**,**
		$(p_1 = 0.07)$, $\omega_s = 9.44$	**97I,99Y,114R,**116D,**151H,152A,156R,163R**
NR	M0	$\omega = 0.93$	None
	M1	$p_0 = 0.76$, $p = 0.24$, $\omega_0 = 0.06$, $\omega_1 = 1$	Not allowed
	M2	$p_0 = 0.63$, $p_1 = 0.30$, $p_2 = 0.07$	**9F,62Q,63E,66N,70H,76A,77N,81L,97I,**
		$\omega_0 = 0.09$, $\omega_1 = 1$, $\omega = 8.54$	**99Y,114R,151H,152A,156R,163R,**167G
	M7	$p = 0.02$, $q = 0.03$	Not allowed
	M8	$p_0 = 0.93$, $p = 0.02$, $q = 0.02$	**9F,62Q,63E,66N**,**70H**,**76A,77N**,**81L**,**97I**
		$(p_1 = 0.07)$, $\omega_s = 9.11$	**99Y**,**114R,151H,152A,156R,163R,** 167G

NOTE.- F3x4, initial $k = 2$; positively selected sites by the BEB method were identified based on the $p > 95\%$ criterion. Sites with $p > 99\%$ are in bold. p_0, p_1, p_2, ω_0, ω_1, ω_S proportions of sites within each category of ω values (purifying selection, neutral evolution, positive selection); p e q, shape parameters for the beta distribution of M7; value estimated from data under M8. Letters attached to the site positions refer to the aminoacid present in that position in the reference sequence for the locus. R, data set with recombinants; NR, data set after removal of recombinants.

Table S11: Parameter estimates under site models for *HLA-B*

Data set	Model	Parameter estimates	Sites with $\omega > 1$
R	M0	$\omega = 0.77$	None
	M1	$p_0 = 0.83$, $p = 0.17$, $\omega_0 = 0.02$, $\omega_1 = 1$	Not allowed
	M2	$p_0 = 0.796$, $p_1 = 0.13$, $p_2 = 0.07$	**24S,45E,63N,67Y,70Q,71A,74D,77S,**
		$\omega_0 = 0.03$, $\omega_1 = 1$, $\omega = 7.66$	**80N,81L,**82R,**94T,95L,97S,113H,**
			114D,116Y,152E,156R,163E,305A
	M7	$p = 0.01$, $q = 0.02$	Not allowed
	M8	$p_0 = 0.93$, $p = 0.01$, $q = 0.05$	**24S,45E,63N,67Y,**69A,**70Q,71A,74D,**
		$(p_1 = 0.07)$, $\omega_s = 8.098$	**77S,80N,81L,82R,94T,95L,97S,113H,**
			114D,116Y,152E,156R,163E,305A
NR	M0	$\omega = 0.86$	None
	M1	$p_0 = 0.83$, $p = 0.17$, $\omega_0 = 0.02$, $\omega_1 = 1$	Not allowed
	M2	$p_0 = 0.77$, $p_1 = 0.14$, $p_2 = 0.09$	**9Y,11S,**12V,24S,**45E,63N,67Y,70Q,71A,**
		$\omega_0 = 0.02$, $\omega_1 = 1$, $\omega = 9.64$	**74D,77S,80N,81L,82R,83G,95L,97S,99Y,**
			113H,114D,**116Y,**152E,**156R,163E,171Y,**305A
	M7	$p = 0.01$,$q = 0.09$	Not allowed
	M8	$p_0 = 0.91$ $p = 0.02$ $q = 0.14$	**9Y,11S,12V,24S,45E,63N,67Y,**69A,**70Q,71A,74D,**
		$(p_1 = 0.09)$ $\omega_s = 9.48$	**77S,80N,81L,82R83G,95L,97S,99Y,113H,**
			114D,116Y,152E,156R,163E,167W,**171Y,305A**

NOTE.- F3x4; initial $k = 2$; positively selected sites by the BEB method were identified based on the $p > 95\%$ criterion. Sites with $p > 99\%$ are in bold. p_0, p_1,p_2, ω_0, ω_1,ω_S proportions of sites within each category of ω values (purifying selection, neutral evolution, positive selection); p e q, shape parameters for the beta distribution of M7; value estimated from data under M8. Letters attached to the site positions refer to the aminoacid present in that position in the reference sequence for the locus. R, data set with recombinants; NR, data set after removal of recombinants.

Table S12: Parameter estimates under site models for *HLA-C*

Data set	Model	Parameter estimates	Sites with $\omega > 1$
R	M0	$\omega = 0.73$	None.
	M1	$p_0 = 0.74$, $p = 0.26$, $\omega_0 = 0.04$, $\omega_1 = 1$	Not allowed
	M2	$p_0 = 0.65$, $p_1 = 0.32$, $p_2 = 0.03$	**9F,24S,73T,**77S,80N**,99C,116Y,156R,163T**
		$\omega_0 = 0.03$, $\omega_1 = 1$, $\omega = 9.8$	
	M7	$p = 0.01$, $q = 0.02$	Not allowed
	M8	$p_0 = 0.97$, $p = 0.005$, $q = 0.01$	**9F,24S,73T,77S,80N,99C,116Y,156R,163T**
		$(p_1 = 0.03)$, $\omega_S = 10.47$	
NR	M0	$\omega = 0.74$	None
	M1	$p_0 = 0.69$, $p = 0.31$, $\omega_0 = 0.04$, $\omega_1 = 1$	Not allowed
	M2	$p_0 = 0.69$, $p_1 = 0.31$, $p_2 = 0.00$	9F, 24S, 73T, **77S**, **80N**, **116Y, 156R, 163T**
		$\omega_0 = 0.04$, $\omega_1 = 1$, $\omega = 999^a$	
	M7	$p = 0.02, q = 0.03$	Not allowed
	M8	$p_0 = 0.95, p = 0.05, q = 0.006$	**9F**,**24S,73T,77S,80N**,**99C**,**116Y,156R,163T**
		$(p_1 = 0.05)$,$\omega_s = 8.79$	

NOTE.- F3x4, initial $k = 2$; positively selected sites by the BEB method were identified based on the $p > 95\%$ criterion. Sites with $p > 99\%$ are in bold. p_0, p_1, p_2, ω_0, ω_1,ω_S proportions of sites within each category of ω values (purifying selection, neutral evolution, positive selection); p e q, shape parameters for the beta distribution of M7; value estimated from data under M8. Letters attached to the site positions refer to the aminoacid present in that position in the reference sequence for the locus. R, data set with recombinants; NR, data set after removal of recombinants.

Table S13: Correlations between pairwise $dN/dS_{\texttt{ARS}}$ and divergence ($dS_{\texttt{non-ARS}}$)

Locus	Spearman	Kendall	Pearson
HLA-A	0.12*(0.22*)	0.08*(0.14*)	0.17*(0.25*)
HLA-B	0.20*(0.19*)	0.14*(0.13*)	0.20*(0.12*)
HLA-C	0.26*(0.24*)	0.18*(0.16*)	0.20*(0.19*)

* $P < 0.001$ obtained by Mantel test.

NAs handled by casewise deletion.

In parentheses: values for NR data sets.

Table S14: Branch models likelihood convergence for *HLA-A* (ARS; NR)

Frequency Model	Initial ω	Model 0 (lnl; ω)	Model 2a (lnl; ω_w; ω_b)	Model 2b (lnl; ω_{tip}; ω_{int})
Fequal	0.2	-946.16; $\omega = 4.59$	-946.15; $\omega_w = 4.34$; $\omega_b = 4.88$	-948.55; $\omega_t = 6.91$; $\omega_i = 3.77$
	0.4	-946.16; $\omega = 4.59$	-946.15; $\omega_w = 4.34$; $\omega_b = 4.88$	-945.92; $\omega_t = 3.43$; $\omega_i = 5.95$
	0.6	-946.16; $\omega = 4.59$	-946.15; $\omega_w = 4.34$; $\omega_b = 4.88$	-945.92; $\omega_t = 3.43$; $\omega_i = 5.95$
	0.8	-946.16; $\omega = 4.59$	-946.15; $\omega_w = 4.34$; $\omega_b = 4.88$	-945.92; $\omega_t = 3.43$; $\omega_i = 5.95$
F1x4	0.2	-943.60;$\omega = 4.23$	-943.59; $\omega_w = 4.01$; $\omega_b = 4.47$	-945.30; $\omega_t = 6.25$; $\omega_i = 3.50$
	0.4	-943.60;$\omega = 4.23$	-943.59; $\omega_w = 4.01$; $\omega_b = 4.47$	-947.898; $\omega_t = 6.75$; $\omega_i = 3.82$
	0.6	-943.60; $\omega = 4.23$	-943.59; $\omega_w = 4.01$; $\omega_b = 4.47$	-947.898; $\omega_t = 6.75$; $\omega_i = 3.82$
	0.8	-943.60;$\omega = 4.23$	-943.59; $\omega_w = 4.01$; $\omega_b = 4.47$	-947.898; $\omega_t = 6.75$; $\omega_i = 3.82$
F3x4	0.2	-935.21; $\omega = 1.84$	-935.18; $\omega_w = 1.68$; $\omega_b = 2.03$	-934.96; $\omega_t = 1.39$; $\omega_i = 2.35$
	0.4	-935.21; $\omega = 1.84$	-935.18; $\omega_w = 1.68$; $\omega_b = 2.03$	-934.96;$\omega_t = 1.39$; ω_i =2.35
	0.6	-935.21;$\omega = 1.84$	-935.18; $\omega_w = 1.68$; $\omega_b = 2.03$	-934.96; $\omega_t = 1.39$; $\omega_i = 2.35$
	0.8	-935.21; $\omega = 1.84$	-935.18; $\omega_w = 1.68$; $\omega_b = 2.03$	-934.96; $\omega_t = 1.39$; $\omega_i = 2.35$
Fcodon	0.2	-910.02; $\omega = 1.82$	-909.91; $\omega_w = 1.59$; $\omega_b = 2.17$	-910.01; $\omega_t = 1.74$; $\omega_i = 1.89$
	0.4	-910.02; $\omega = 1.82$	-909.91; $\omega_w = 1.59$; $\omega_b = 2.17$	-910.01; $\omega_t = 1.74$; $\omega_i = 1.89$
	0.6	-910.02; $\omega = 1.82$	-909.91; $\omega_w = 1.59$; $\omega_b = 2.17$	-910.01; $\omega_t = 1.74$; $\omega_i = 1.89$
	0.8	-910.02; $\omega = 1.82$	-909.91; $\omega_w = 1.59$; $\omega_b = 2.17$	-910.01 ; $\omega_t = 1.74$; $\omega_i = 1.89$

Model 2a: within/between; Model 2b: terminal/internal; lnl, log likelihood. NR, data set after removal of recombinants.

Table S15: Branch models likelihood convergence for *HLA-B* (ARS; NR)

Model	Initial ω	Model 0 (lnl; ω)	Model 2a (lnl; ω_w; ω_b)	Model 2b (lnl; ω_{tip}; ω_{int})
Fequal	0.2	-1159.28; $\omega = 2.79$	-1158.96;$\omega_w = 2.08$; $\omega_b = 3.26$	-1158.77; $\omega_t = 1.9$; $\omega_i = 3.38$
	0.4	-1159.28; $\omega = 2.79$	-1158.96; $\omega_w = 2.08$; $\omega_b = 3.26$	-1158.77; $\omega_t = 1.9$; $\omega_i = 3.38$
	0.6	-1159.28; $\omega = 2.79$	-1158.96; $\omega_w = 2.08$; $\omega_b = 3.26$	-1158.77; $\omega_t = 1.9$; $\omega_i = 3.38$
	0.8	-1159.28; $\omega = 2.79$	-1158.96; $\omega_w = 2.08$; $\omega_b = 3.26$	-1158.77; $\omega_t = 1.9$; $\omega_i = 3.38$
F1x4	0.2	-1159.21; $\omega = 2.58$	-1158.87; $\omega_w = 1.95$; $\omega_b = 2.99$	-1158.75; $\omega_t = 1.79$; $\omega_i = 3.11$
	0.4	-1159.21; $\omega = 2.58$	-1158.93;$\omega_w = 1.95$; $\omega_b = 2.99$	-1158.87; $\omega_t = 1.95$; $\omega_i = 2.99$
	0.6	-1159.16; $\omega = 2.58$	-1158.93; $\omega_w = 1.95$; $\omega_b = 2.99$	-1158.87; $\omega_t = 1.95$; $\omega_i = 2.99$
	0.8	-1159.16; $\omega = 2.58$	-1158.93;$\omega_w = 1.95$; $\omega_b = 2.99$	-1158.87; $\omega_t = 1.95$; $\omega_i = 2.99$
F3x4	0.2	-1112.27; $\omega = 0.99$	-1111.91; $\omega_w = 0.73$; $\omega_b = 1.16$	-1111.78; $\omega_t = 0.69$; $\omega_i = 1.2$
	0.4	-1112.27; $\omega = 0.99$	-1111.91; $\omega_w = 0.73$; $\omega_b = 1.16$	-1111.78; $\omega_t = 0.69$; $\omega_i = 1.2$
	0.6	-1112.27; $\omega = 0.99$	-1111.91; $\omega_w = 0.73$; $\omega_b = 1.16$	-1111.78; $\omega_t = 0.69$; $\omega_i = 1.2$
	0.8	-1112.27; $\omega = 0.99$	-1111.91; $\omega_w = 0.73$; $\omega_b = 1.16$	-1111.78; $\omega_t = 0.69$; $\omega_i = 1.2$
Fcodon	0.2	-1088.75; $\omega = 1.88$	-1088.27; $\omega_w = 1.3$; $\omega_b = 2.29$	-1089.39; $\omega_t = 1.20$; $\omega_i = 2.36$
	0.4	-1088.75; $\omega = 1.88$	-1088.27; $\omega_w = 1.3$; $\omega_b = 2.29$	-1089.8; $\omega_t = 1.27$; $\omega_i = 2.31$
	0.6	-1090.33; $\omega = 1.88$	-1088.27; $\omega_w = 1.3$; $\omega_b = 2.29$	-1088.76; $\omega_t = 1.20$; $\omega_i = 2.35$
	0.8	-1088.75; $\omega = 1.88$	-1089.84; $\omega_w = 1.30$; $\omega_b = 2.29$	-1088.11; $\omega_t = 1.22$; $\omega_i = 2.34$

Model 2a: within/between; Model 2b: terminal/internal; lnl, log likelihood. NR, data set after removal of recombinants.

Table S16: Branch models likelihood convergence for *HLA-C* (ARS; NR)

Model	Initial ω	Model 0 (lnl; ω)	Model 2a (lnl; ω_w; ω_b)	Model 2b (lnl; ω_t; ω_i)
Fequal	0.2	-946.76;$\omega = 4.47$	-946.89; $\omega_w = 2.77$; $\omega = 9.6$	-944.33; $\omega_t = 2.12$; $\omega_i = 11.57$
	0.4	-946.76;$\omega = 4.47$	-945.49;$\omega_w = 2.77$; $\omega_b = 9.6$	-944.33; $\omega_t = 2.12$; $\omega_i = 11.57$
	0.6	-946.76;$\omega = 4.47$	-946.89; $\omega_w = 2.77$; $\omega_b = 9.6$	-944.33; $\omega_t = 2.12$; $\omega_i = 11.57$
	0.8	-946.76;$\omega = 4.47$	-946.89; $\omega_w = 2.77$; $\omega_b = 9.6$	-944.33; $\omega_t = 2.12$; $\omega_i = 11.57$
F1x4	0.2	-960.73;$\omega = 4.04$	-959.47; $\omega_w = 2.51$; $\omega_b = 8.66$	-958.44; $\omega_t = 1.97$;$\omega_i = 10.29$
	0.4	-960.73;$\omega = 4.04$	-959.47; $\omega_w = 2.51$; $\omega_b = 8.66$	-959.47; $\omega_t = 2.51$; $\omega_i = 8.66$
	0.6	-960.73;$\omega = 4.04$	-959.47; $\omega_w = 2.51$; $\omega_b = 8.66$	-959.47; $\omega_t = 2.51$; $\omega_i = 8.66$
	0.8	-960.73;$\omega = 4.04$	-959.47; $\omega_w = 2.51$; $\omega_b = 8.66$	-959.47; $\omega_t = 2.51$; $\omega_i = 8.66$
F3x4	0.2	-951.50;$\omega = 1.89$	-950.199;$\omega_w = 1.19$; $\omega_b = 4.14$	-947.82;$\omega_t = 0.95$; $\omega_i = 4.91$
	0.4	-951.50;$\omega = 1.89$	-950.199 $\omega_w = 1.19$; $\omega_b = 4.14$	-947.82; $\omega_t = 0.95$; $\omega_i = 4.91$
	0.6	-951.50;$\omega = 1.89$	-950.199 $\omega_w = 1.19$; $\omega_b = 4.14$	-947.82; $\omega_t = 0.95$; $\omega_i = 4.91$
	0.8	-951.50;$\omega = 1.89$	-950.199; $\omega_w = 1.19$; $\omega_b = 4.14$	-947.82; $\omega_t = 0.95$; $\omega_i = 4.91$
Fcodon	0.2	-900.96;$\omega = 2.99$	-899.56; $\omega_w = 1.8$; $\omega_b = 6.65$	-898.68; $\omega_t = 1.46$; $\omega_i = 7.67$
	0.4	-900.96;$\omega = 2.99$	-899.56 ; $\omega_w = 1.8$; $\omega_b = 6.65$	-898.68; $\omega_t = 1.46$; $\omega_i = 7.67$
	0.6	-900.96;$\omega = 2.99$	-899.56; $\omega_w = 1.8$; $\omega_b = 6.65$	-898.68; $\omega_t = 1.46$; $\omega_i = 7.67$
	0.8	-900.96;$\omega = 2.99$	-899.56; $\omega_w = 1.8$; $\omega_b = 6.65$	-898.68; $\omega_t = 1.46$; $\omega_i = 7.67$

Model 2a: within/between; Model 2b: terminal/internal; lnl, log likelihood. NR, data set after removal of recombinants.